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CXCL9/CXCL10 as biomarkers the monitoring of treatment responses in Pulmonary TB patients: a systematic review and meta-analysis

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Summary

Background Tuberculosis (TB) remains a persistent threat to global public health and traditional treatment monitoring approaches are limited by their potential for contamination and need for timely evaluation. Therefore, new biomarkers are urgently required for monitoring the treatment efficacy of TB.

Methods This study aimed to elucidate the levels of CXCL10 and CXCL9 in pulmonary TB patients who underwent anti-TB treatment. The data was acquired from five databases, including PubMed, Ovid, Web of Science, Embase, and the Cochrane Library. A meta-analysis of CXCL10 data from all time points was conducted. Furthermore, a trend meta-analysis of temporal data of CXCL10 and CXCL9 from multiple time points was also performed.

Results It was revealed that patients who responded poorly to anti-TB treatment had higher serum levels relative to those who responded well (SMD: 1.23, 95% CI: -0.37–2.84) at the end of intensive treatment (2 months). Furthermore, heterogeneity was observed in these results, which might be because patients with a prior history of TB and different treatment monitoring methods than those selected in this study were also included. The analysis of alterations in CXCL10 and CXCL9 levels since the last collection time points indicated that their levels reduced with time.

Conclusion In summary, the study revealed that reductions in CXCL10 levels during the first two months of anti-TB treatment are correlated with treatment responses. Furthermore, decreasing levels of CXCL9 during the treatment suggest that it may also serve as a biomarker with a similar value to CXCL10. Future in-depth studies are thus warranted to further probe the relevance of CXCL10 and CXCL9 in monitoring the treatment efficacy of TB.

Keywords Tuberculosis, PTB, Interferon-Inducible protein 10, Chemokine CXCL9, Treatment response

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Introduction

Tuberculosis (TB) is a mycobacterial infection caused by *Mycobacterium tuberculosis*. It is the second most prevalent cause of chronic respiratory disease in the world. The 2023 TB report published by the World Health Organization (WHO) [1] indicated that the global effects of the COVID-19 pandemic had adversely impacted TB patient diagnosis and treatment efforts in 2022, with treatment success rates of 88% and 63% for patients with drug-susceptible TB and multidrug-resistant/rifampicin-resistant TB, respectively. Techniques that can efficiently and early diagnose TB as well as monitor the treatment effect in patients are essential for ensuring efficacious treatment outcomes and preventing the emergence of resistant disease. However, currently, the monitoring of patients undergoing anti-TB treatment is a clinical challenge.

The WHO endorses sputum microscopy and culture as the primary approaches for monitoring TB patient treatment responses [2]. During the treatment, smears and cultures are routinely evaluated every month to assess patient responses to current treatment. Patients who exhibit persistent microbiological positivity at 2 months post-treatment evaluation are classified as slow responders, indicating a poor response to anti-TB therapy. Conversely, patients who achieve microbiological conversion within 2 months of treatment are classified as fast responders. However, these microbiology-based methods have some significant limitations, such as they markedly rely on the sputum sample collection, which is associated with a substantial risk of contamination from the oral cavity and upper respiratory tract. Furthermore, in some patients, the sputum collection process can be challenging such as in children. Moreover, the time-related restrictions and increased analytical timelines of sputum microscopy and culture methods also render them suboptimal for the rapid evaluation of patient treatment responses, thereby slowing the clinical decision-making for appropriate treatment regimens. Recently, several new promising biomarkers have been identified with high specificity and sensitivity for the monitoring of TB patient treatment outcomes, including RISK6 (mRNA signature 6-Marker), TB22 (mRNA signature 22-Marker), Lipoarabinomannan (LAM), etc [3–7].

There are certain inherent limitations to the use of monitoring methods that are reliant on particular omics approaches. While genomic markers can be extremely powerful, they are also very costly such that their widespread adoption in primary diagnostic and monitoring of a disease is infeasible, particularly in developing countries. The monitoring of the treatment outcomes in TB patients using transcriptomic data derived from different sequencing platforms or technologies can yield inconsistent data; therefore, larger sample sizes are necessary to establish universal standards. Thus, cost-effective and practical biomarkers for the time-sensitive monitoring of TB patient's treatment efficacy are urgently required.

CXCL10 and CXCL9 are the members of the CXC chemokine family that are crucial regulators of cellular migration and inflammatory responses [8]. CXCL10 and CXCL9 exert their biological effects *via* CXCR3 signaling and trigger downstream immune activity [9, 10]. In pulmonary TB, CXCL9 and CXCL10 play crucial roles in recruiting chemotactic activated/effector cells to the site of TB infection, facilitating the formation of TB granulomas [11]. Their secretion is regulated by IFN-γ, which plays a key role in the immune response to TB. During effective anti-TB treatment, the pathogen load reduces, the inflammatory response in the body gradually weakens, and the level of IFN-γ decreases accordingly, which in turn reduces the levels of CXCL9 and CXCL10 [12, 13]. During TB progression, the patient's serum CXCL9 and CXCL10 levels increase more than the healthy control individuals or those diagnosed with other pulmonary diseases [14–16]. Both CXCL10 and CXCL9 have been explored as auxiliary biomarkers to distinguish between patients with active and latent TB infection [12, 17, 18]. Although studies have indicated that the levels of CXCL9 and CXCL10 may guide clinical decision-making when monitoring patient treatment responses [19–21], there are only a few quantitative analyses on the relationship between CXCL9 and CXCL10 levels and anti-TB treatment response monitoring.

This systematic review and meta-analysis comprehensively analyzed CXCL9 and CXCL10 as a monitoring tool for anti-TB treatment outcomes. Furthermore, this study examines the relationship between CXCL9 and CXCL10 levels and treatment response in patients undergoing anti-TB therapy. The primary endpoint of the study was the microbiological and clinical outcome at 2 months post-treatment, while the secondary endpoint included longitudinal trends of CXCL9 and CXCL10 levels at various time points during treatment. Overall, this study aimed to address: (1) The correlation between CXCL9 and CXCL10 levels and the treatment response and (2) The longitudinal changes in CXCL9 and CXCL10 levels in in pulmonary TB patients throughout anti-TB treatment.

Methods

This study conducted a systematic review and meta-analysis of serum CXCL9 (MIG) and CXCL10 (IP-10) levels in pulmonary TB patients undergoing standard anti-TB treatment. The study selection criteria were based on the PRISMA checklist [22] (Table S1), and the PROSPERO (CRD42023480875) protocol was employed.

Search strategy

Studies were retrieved from the PubMed, Embase, Web of Science, Ovid, and Cochrane Library databases using the following search terms: (Tuberculosis or TB or Multidrug-Resistant Tuberculosis or tuberculosis Infection or XDR-TB OR LTBI) AND (Treatment Outcome or Efficacy or Treatment Effectiveness or Treatment response or monitor) AND (Chemokine CXCL9 or 'Monokine Induced by gamma Interferon Chemokine' or MIG or Small Inducible Cytokine B9 SCYB9 Chemokine) AND (Chemokine CXCL10 or CXCL10 or Cytokine IP-10 Protein or IP-10 OR 'interferon-gamma-Inducible Protein of 10 kDa').

Eligibility criteria

All studies published in English from January 1, 2005, to May 31, 2023, were eligible for inclusion in this meta-analysis. Inclusion criteria included (i) cross-sectional, cohort, and case-control as well as randomized controlled trials (RCTs), (ii) studies focused on changes in the levels of particular biomarkers during anti-TB treatment, (iii) studies on diagnosed TB patients, confirmed through bacteriological analysis, and (iv) studies with no age restrictions for patients but with a minimum of two-time points follow-up data during treatment. Exclusion criteria included: (i) studies on latent *M. tuberculosis* infections and non-tuberculous mycobacteria associated with other respiratory diseases, (ii) epidemiological studies, (iii) studies with patients who were only tested after initiating treatment, (iv) studies only focused on non-serum samples (such as pulmonary biopsy samples), (v) studies which analyzed stimulated CXCL10 levels, (vi) narrative or systematic reviews, meta-analyses, comments, conference abstracts, case reports, animal studies, editorials, or full-text articles that were not published in English, and vi) studies which employed non-standard therapeutic test references or acceptable reference standards including the culture of *M. tuberculosis*, Xpert MTB/RIF, smear microscopy, and clinical manifestations.

The patient's recruitment was not restricted to any particular geographic region or type of healthcare system.

Study selection and risk of bias measurement

EndNote (version X9) was used to manage and evaluate all the selected studies, which were independently reviewed by two investigators (Z.Y. and J.Y.) who read the full text of potentially relevant articles and extracted the data. Of 267 studies, 251 were removed as duplicates after abstract/title and full-text review, while 16 were included for data extraction from full text. Two investigators (Z.Y. and J.Y.) independently scored all 16 articles using the QUADAS-2 tool [23] to assess their methodological quality. In case of any discrepancy, a third investigator (M.F.) resolved the issue after discussion and mutual consensus.

Data extraction

Before data extraction, two investigators (Z.W. and Y.C.) performed a thorough feasibility analysis of the established data extraction forms by randomly selecting the included studies. A third investigator (F.M.) was consulted in cases of disagreements between these authors. The data extraction form included: (i) basic information such as the origin country of the study, number of participants, baseline patient information, follow-up time points, and (ii) cytokine levels (average/median), as well as difference measurements (standard deviation, interval range) during each follow-up period. These data were independently extracted from the full text of the 16 included studies by two authors. In case no quantitative data were provided and could not be obtained after contacting the original authors, a third author (ZW) extracted graphical data from these studies. This approach was accepted only for extracting data from corresponding graphs [24, 25]. Extraction feasibility was assessed based on both article design reliability and graph extraction feasibility. When data were extracted from these figures, they were independently extracted by two investigators (Z.W. and Y.C.), and the average values were retained for analysis.

Data analysis

Following the data extraction and the assessments of central tendency and spread of these data at different follow-up time points, the extracted data were combined to produce standardized sample mean and standard deviation values and to assess corresponding trends. This study estimated normalized sample means and standard deviations using a data processing tool and employing the formulas provided by Wan et al. [26]. This approach integrates sample size with median, minimum, maximum, and/or interquartile range values to yield more accurate estimates. Since the follow-up times were varied in the studies, fold-change values for the analyzed biomarkers were measured relative to the previous collection time point, consistent with the report of Zimmer et al. [27].

To comprehensively analyze the changes in CXCL9/CXCL10 levels during treatment, this study employed two different analytical approaches. The first comprised a meta-analysis of all time points for CXCL9/CXCL10 levels, which was conducted using a random-effects model with a standardized mean difference (SMD) as the effect size. Patients who remained bacteriologically positive two months after anti-TB treatment (slow responders) were selected as the experimental groups. The control group comprised patients who were bacteriologically negative two months after initiating treatment (fast responders).

The second approach of the study included a trend meta-analysis of CXCL9/CXCL10 levels during the treatment, which was conducted using a random intercept model. The estimated fold-change in CXCL9/CXCL10 levels was calculated with corresponding 95% confidence intervals (CIs). Covariance matrices and log-fold changes were calculated for each study through multivariate normal distribution simulations. Data were integrated using block diagonal matrix methods, and random intercept models were employed to analyze potential random effects. Furthermore, treatment responses for TB patients newly diagnosed using positive sputum smear test at the start of treatment were determined based on smear results before entrance into the treatment consolidation phase. Whereas, treatment responses for TB patients newly diagnosed using negative microscopic sputum smear test at the start of treatment were primarily based on risk factor scores or symptom scores.

The I^2 statistic was employed to assess heterogeneity, and the outlier studies were identified using Galbraith plot analyses when assessing bias in research publications using the trim-and-fill method [28, 29]. A sensitivity analysis was also performed *via* an impact analysis by excluding or not excluding the study published by Annalisa et al. [30]. The heterogeneity in the literature was addressed through sensitivity analysis exclusion. For the meta-analysis of all time points, covariates such as patient age, history of tuberculosis, cytokine detection methods, and HIV history were introduced. Furthermore, a Meta-regression approach was employed to analyze sources of heterogeneity [31]. Significant differences were identified based on a two-sided $p<0.05$. STATA 14.0 and R v4.2.2 were used for all statistical analyses [32].

Results

Study selection

Of 601 studies identified using the initial search strategy, 334 were duplicates and excluded from further examination. After a full-text review of the remaining 228 studies, 212 were excluded, while 16 were retained for analysis (Fig. 1) [30, 33–47]. Of the 212 excluded studies, 93 were excluded as they were not focused on treatment monitoring or other cytokines analysis, 42 were focused on non-TB mycobacteria or other respiratory diseases, and 29 were diagnostic tests or in vitro assays. Epidemiological analyses were also excluded from this study ($n=7$). The remaining 16 studies were included in the quantitative synthesis and meta-analysis. Only 2 of these studies provided quantitative data on CXCL9 levels.

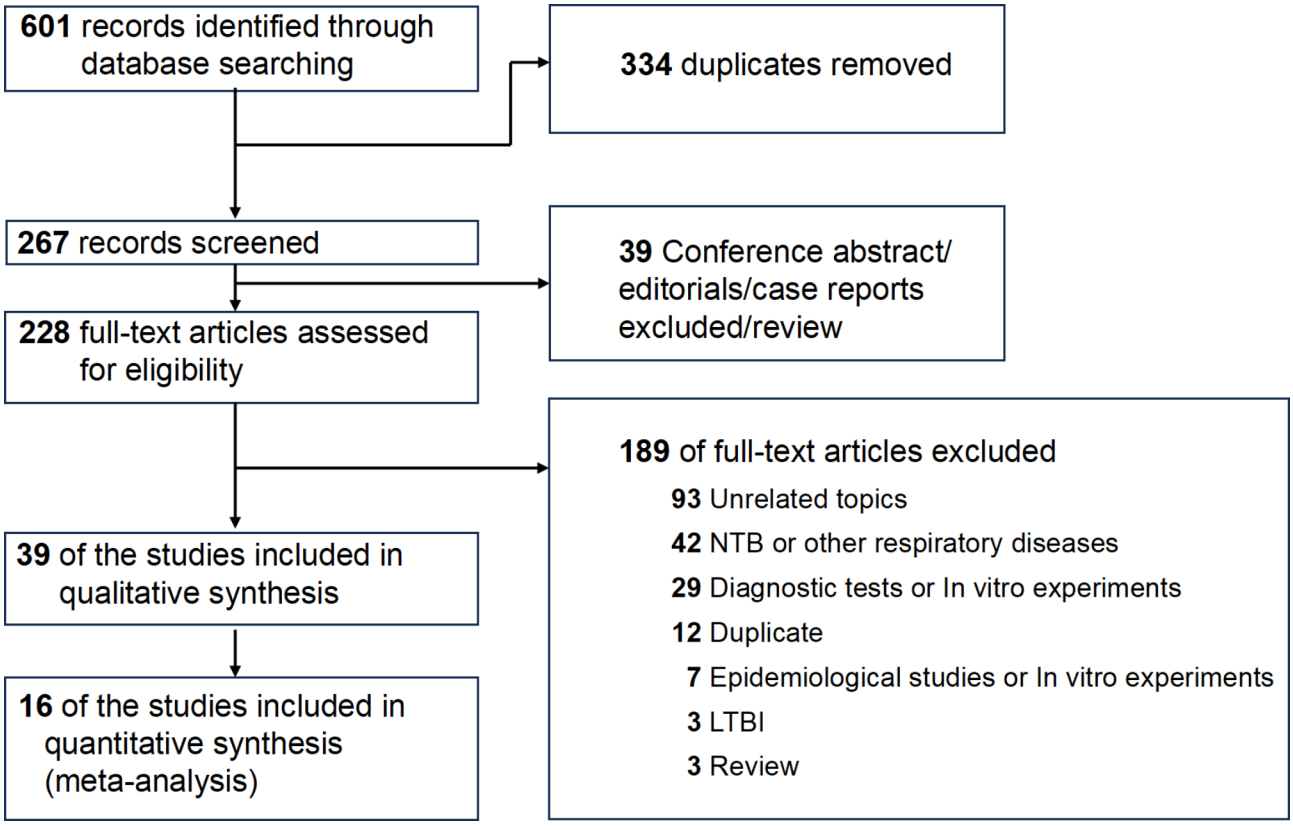

Fig. 1 PRISMA flow chart for the study selection process

Study characteristics

Of the 16 studies included in this meta-analysis, 14 were prospective analyses [38, 46]. The demographic characteristics of the patients from these 16 studies are presented in Table S2. These 14 studies were conducted in 8 different countries/regions, of which 14 were performed in a single country, while 2 were multicenter (bicentric) studies [44, 46]. Furthermore, 10 studies were performed in countries with moderate to high TB prevalence. Only one study included children [47]. Age ranges varied substantially among studies. Moreover, 5 studies did not report data related to HIV status, while ~ 50% of patients in one study were HIV-positive [44]. In 68% of the studies, the patient's TB history was not documented. ELISAs were used to measure CXCL9/CXCL10 levels in 10 studies, while the remaining studies employed commercial Luminex kits or cell counting bead arrays (CBA). In addition, 7 studies classified patients as slow or fast responders when evaluating their reactions to conventional anti-TB treatment.

Quality and risk of bias assessment

The QUADAS-2 tool was employed to assess the potential risk of bias and quality of the included studies, with sources of potential bias classified into four distinct categories: "patient selection", "index testing", "reference standard" and "flow and timing" [23]. The majority of the included studies were prospective cohort studies, with 4 exhibiting a low risk of bias (Figure S2). Those studies in which healthy controls were included as a control group indicated a higher risk of patient selection bias and a generally higher overall risk of bias ($N=2$) or a risk of bias classified as "unclear" (Figure S1). The generally higher overall risk of the two studies was primarily due to unclear referencing standards, procedural ambiguities, and timing issues. Most studies failed to directly observe or document patient's compliance-related support measures. Just one study employed a double-blind approach when referencing criteria to interpret index results. Furthermore, 2 studies indicated a high degree of "flow and timing" risk, while the other studies revealed a generally low risk of bias (Fig. 2). As these were prospective cohort studies, all patients were subjected to the same criteria, and sample collection and processing were performed promptly.

Comparisons between slow responders and fast responders

Since the design of most included studies varied, quantitative data on CXCL10 levels in slow and fast responders

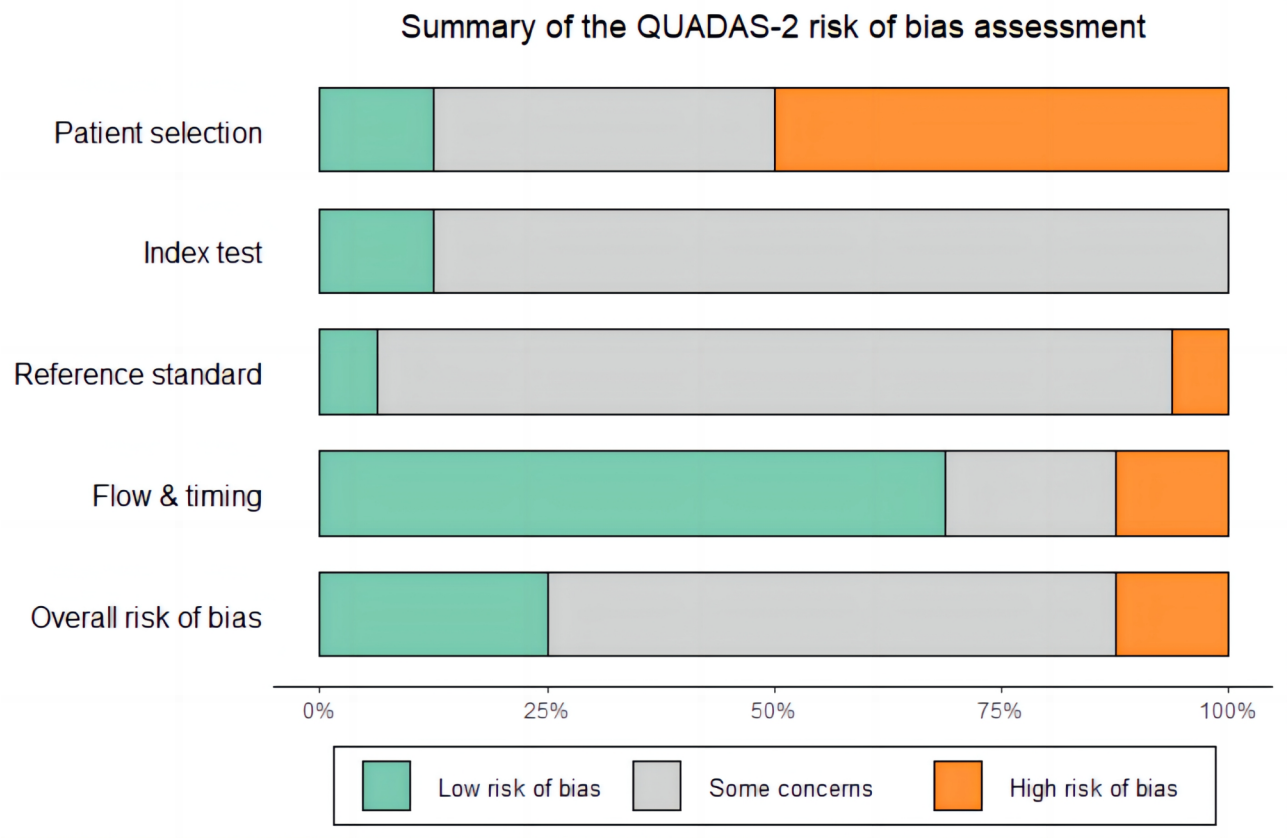

Fig. 2 QUADAS-2 risk of bias assessment results

were only reported by 5 studies. Furthermore, CXCL9 data of slow and fast responders was only reported by 2 studies and therefore, was insufficient for any meta-analysis (Table S2). Comprehensive details of these 5 studies' results are presented in Fig. 3. Elevated baseline (0 M) levels of CXCL10 were associated with a higher chance of a poor TB treatment response, with a pooled Standardized Mean Difference value of 0.45 (95% CI: 0.17–0.72). No significant differences were observed between the 2- and 6-month (2 M and 6 M) patient subgroups, which might be because of the high heterogeneity levels at these time points (2M: I^2= 96.3%, *p-value* < *0.001*; 6M: I^2= 99.3%, *p-value*<*0.001*).

A sensitivity analysis was conducted to explain the observed heterogeneity, which excluded the study by Annalisa (2005) as it had a significantly skewed effect size relative to other studies (Figure S2). Meta-regression results indicated that TB history was a source of heterogeneity (*p=0.016*), whereas age, testing approach, and HIV were not the sources of significant heterogeneity (Figure S3). After excluding the study of Annalisa (2005), the overall heterogeneity decreased markedly (Figure S4). In the 2 M subgroup, high CXCL10 levels were linked to a greater chance of an unfavorable TB treatment response, with a pooled Standardized Mean Difference of 0.55 (95% CI: 0.02–1.08; I^2 = 49.0%, $p > 0.05$). However, at 6 months, no significant differences were observed in CXCL10 levels between the slow and fast responders, with a pooled Standardized Mean Difference of 0 (95% CI: -0.52–0.51; I^2 = 0.0%, *p-value = 0.605*).

CXCL9 and CXCL10 trend meta-analysis

The levels of CXCL9 and CXCL10 during the treatment were also evaluated through a trend meta-analysis, which compared these levels to previous time points. A meta-analysis of these results indicated that the fold-change values of CXCL9 and CXCL10 levels declined relative to previously recorded values (Table 1). Overall, this analysis included 11 and 4 studies focused on CXCL10 and CXCL9, with the fold change of -20.2 (95% CI: -56.4 to -16.6) and −28.3 (95% CI: -40.1 to -16.7), respectively. The maximal fold-change values for CXCL10 and CXCL9

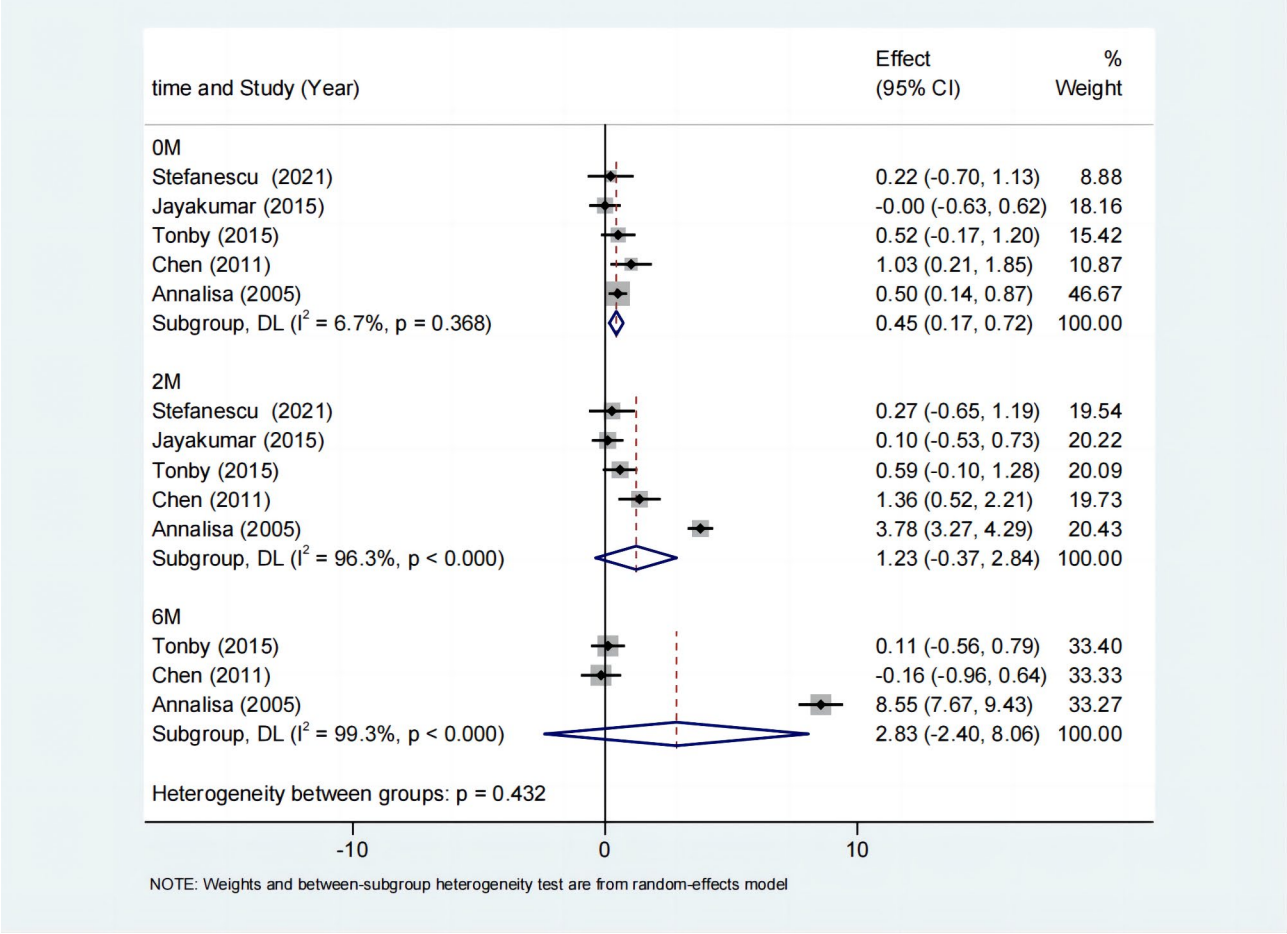

Fig. 3 Forest plots for SMD values comparing the levels of CXCL10 between slow and fast responders at 0, 2, and 6 months of treatment
CXCL10: IFN-gamma-Inducible Protein, 10 kDa; TB: tuberculosis; SMD: standardized mean difference

Table 1 Combined sensitivity analysis (ρ) of weekly fold-change meta-regression and pooled fold-change data pertaining to the serum levels of CXCL9 and CXCL10 during anti-TB treatment

	Data from the time point recorded			Correlation coefficient (ρ) (95% CI)			
Cytokine	**Studies**	**No. of participants**	**Avg fold change (% [95% CI])**	**0**	**0.25**	**0.5**	**0.75**
CXCL10	11	585	-28.3 (-40.1 to -16.7)	-28.9 (-40.6 to -17.3)	-28.8 (-40.5 to -17.2)	-28.1 (-39.9 to -16.4)	-27.5 (-39.3 to -15.7)
CXCL9	4	479	-20.2 (-56.4 to -16.6)	-21.9 (-58.3 to -14.4)	-20.4 (-56.9 to -16.1)	-19.3 (-55.3 to -16.8)	-18.5 (-55.0 to -17.9)

CXCL10: Chemokine (C-X-C Motif) Ligand 10 Protein; CXCL9: Chemokine (C-X-C Motif) Ligand 9 Protein; ρ: correlation coefficient; CI: confidence interval

were −69.5% and −64.9%, respectively (Figure S5-6) and both the biomarkers indicated narrow confidence intervals.

Discussion

The objective of this study was to evaluate the levels of CXCL9 and CXCL10 as a standardized monitoring tool for anti-TB treatment responses. CXCL10 is a serological marker and has been investigated in studies focused on the diagnosis, clinical evaluation, and therapeutic monitoring of TB patients [15, 17, 48–52]. There have been several reports demonstrating the diagnostic performance of CXCL9 and CXCL10. For example, Sampath et al. [53] analyzed latent TB, drug-resistant TB (DR-TB), and drug-sensitive TB (DS-TB) patients and compared the differences in CXCL10 and CXCL9 levels between drug-resistant and drug-sensitive patients. DR-TB patients (CXCL9, median: 205.99; CXCL10, median: 1205.75) exhibited significantly increased levels of CXCL9 and CXCL10 compared to DS-TB patients (CXCL9, median: 134.48; CXCL10, median: 650.50). CXCL9 (AUC=0.82, $p<0.0001$) and CXCL10 (AUC=0.84, $p<0.0001$) effectively discriminate DR-TB from DS-TB. The results indicated that these chemokines may differentiate between disease stages. CXCL9 and CXCL10 are both CXC family chemokines that synergistically regulate host immune responses; however, there are only a few studies that have quantitatively assessed their role in therapeutic monitoring [54]. Therefore, this study analyzed these chemokines as biomarkers, and although the results are promising, further comprehensive biomarker-focused studies are required to improve timely and effective treatment monitoring for TB patients.

Quantitative meta-analysis results indicated that the levels of CXCL9 and CXCL10, as measured based on the mean fold-change in chemokine levels, decreased over the course of anti-TB treatment relative to baseline levels. Furthermore, CXCL10 levels were significantly higher in slow responders as compared to fast responders at 2 months of treatment (SMD: 0.55, 95% CI: 0.02–1.08). These results suggest that the level of CXCL10 could serve as an indicator to detect whether microbiological reversal occurs in patients. Analyses of mean fold-change relative to baseline confirmed that both CXCL9 and CXCL10 serum concentrations reduced during intensive treatment phases, with mean fold-changes of -20.2 (95% CI: -56.4 to -16.6) and −28.3 (95% CI: -40.1 to -16.7), respectively, compared to prior analytical time points. Our analysis indicates that CXCL10 levels were not significantly different between slow responders and fast responders at 6 months of treatment. Additionally, there were no discernible differences in microbiological or clinical evaluations between fast and slow responders at 6 months of treatment. This observation is consistent across the included studies and supports the notion that CXCL10 levels, as reported in our study, are concordant with the microbiological examination results. Changes in the levels of CXCL10 and CXCL9 over the course of treatment in individual studies are presented in Figure S5 and Figure S6. CXCL10 demonstrating downward trends with time as compared to baseline, whereas CXCL9 levels tend to increase over time. However, these results are controversial. For example, Chung et al. [37] observed inconsistent increases or decreases in serum CXCL9 levels in slow and fast responders after the treatment, complicating the interpretation of CXCL9's clinical relevance in TB treatment monitoring.

Here, the patient's serum, blood, and/or plasma levels of CXCL9 and CXCL10 were analyzed, which indicates that easy analysis with minimal attendant risk of biohazard exposure or contamination from sample processing. This is a clear advantage over more traditional TB therapeutic monitoring strategies, which often entail sputum culture evaluation [55]. However, the magnitude of change in CXCL9 levels over the course of treatment was limited in this analysis, and substantial heterogeneity was detected among studies, hampering adequate analysis of CXCL9's role in the detection and monitoring of TB.

To date, several studies have indicated novel approaches to monitor TB treatment, including serum-based transcriptomic analyses, metabolomics strategies, and the use of new imaging technologies to evaluate clinical signs and symptoms [56–65]. These approaches hold great promise as do not require sputum sample processing, specifically in a research field [66]. Sigal et al., for

example, screened 70 infection, metabolism, and inflammation-related markers in serum samples collected from 319 pulmonary TB patients [67]. They revealed that the levels of SAA1, PCT, IL-1β, IL-6, CRP, PTX-3, and MMP-8 were strongly correlated with disease severity and early treatment response. However, the data obtained from patients is highly heterogeneous, which interferes with the implementation of similar testing in centralized laboratories and limits effective disease treatment *via* these approaches [68]. The sputum samples may be not required when CXCL9 and CXCL10 are used as therapeutic biomarkers in anti-TB treatment. However, the evidence is currently insufficient to confirm their ability to detect microbiological reversals in patients. The existing literature exhibits substantial variability in research methodologies and designs, complicating result comparisons and integration, and presenting challenges in explaining heterogeneity. Establishing standardized study designs is crucial for future investigations to comprehensively analyze the biomarker properties of CXCL9 and CXCL10. Currently, only one metabolomics analysis on 48 TB patients, 20 TB-DM patients, and 48 non-HIV-infected healthy controls has proposed that analyzing the shifts in metabolic activity during anti-TB treatment has been proposed as a viable treatment monitoring approach [69]. Based on the observed decrease in metabolite levels during the treatment, the authors developed a model (AUC=0.91–0.97) capable of readily differentiating between these three treatment groups of patients. In this study, slow and fast responders were used for the indirect assessment of treatment response, since most clinical efficacy endpoints in the analyzed studies did not include disease recurrence. Currently, a significant concern is the standardization of clinical efficacy.

There are several limitations in this analysis. First, effective meta-analyses of longitudinal data markedly depend on the study's experimental design, potentially contributing to varying levels of bias and possible gaps in the data. To minimize time-related variability, meta-analyses of all time points and trends were included in this study, focusing on fold-change values for CXCL9 and CXCL10 levels in treated TB patients. However, as observed by Zimmer et al. [27], these analytical outcomes depend on the data derived from the included studies, introducing a high risk of bias. Secondly, in this quantitative meta-analysis, data extraction was limited by the lack of data in the form of charts or numerical values in the analyzed studies. The extraction of data from graphs can introduce bias, although prior studies suggest that the overall magnitude of such bias is minor. Although efforts were made to minimize this source of bias, some subjectivity in result interpretation may persist. Third, relatively few relevant articles on CXCL9 were included in this study; therefore, CXCL10 was included in both meta-analyses, while CXCL9 was only included in the trend meta-analysis. Lastly, although limited efforts were made to assess the potential sources of heterogeneity, a wide range of complex factors can contribute to the incidence of heterogeneity. Furthermore, the overall quality of patient screening data in the included studies was not uniform, which might be another major source of potential bias.

Prompt assessment of the patient's treatment response facilitates the formulation of a tailored treatment regimen based on individual circumstances. Fast responders may benefit from regimen adjustments such as shortened treatment duration and reduced drug dosage, which can mitigate the risk of drug-induced hepatotoxicity and serious adverse effects. Whereas, slow responders may indicate inadequate response to anti-TB therapy, indicating an increased risk of drug-resistant TB. Clinicians can rapidly evaluate patient drug resistance, enabling them to review and adjust treatment plans effectively. This includes optimizing drug combinations and dosages in current treatments. Clinicians should consider incorporating second-line drugs such as bedaquiline and fluoroquinolones. If drug resistance is confirmed, they should transition to a regimen recommended for MDR-TB or XDR-TB. Although this study offers new insight that may help guide clinical treatment planning for TB patients, only CXCL9 and CXCL10 were assessed, and the potential performance of other biomarkers warrants further research.

In conclusion, based on the current research in this field, further studies are required to assess the efficacy of utilizing specific chemokines as biomarkers to monitor TB patient treatment responses as there are no established clinical guidelines on their use. This systematic review and meta-analysis explored the potential of CXCL10 and CXCL9 levels as biomarkers for monitoring the treatment response in TB patients and provided a foundation to guide further research efforts in this field.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-09939-0.

Supplementary Material 1

Author contributions

Author contributions: ZW, YC, FM, and YY conceived and designed the study, undertook the review and data abstraction, and drafted the article. PD and YC designed the search strategy. ZW performed statistical analysis. All authors commented on and revised the article.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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